

CLAIMS

What is claimed is:

1. A dry-granulated pharmaceutical composition comprising atorvastatin or a pharmaceutically acceptable salt thereof .
- 5 2. The pharmaceutical composition according to Claim 1 wherein the composition contains less than about 5% (w:w) of an alkaline earth metal salt additive.
3. The pharmaceutical composition according to Claim 1 wherein the dry-granulated composition, after storage at 40°C and 75% relative humidity for 4 weeks, contains not more than about 2% total impurities and/or degradants based on area
10 percent of drug related HPLC peaks.
4. The pharmaceutical composition according to Claim 1 wherein the composition contains not more than about 2% atorvastatin lactone based on area percent of HPLC peaks.
5. The pharmaceutical composition according to Claim 1 wherein the composition is
15 used in the formation of a solid unit dosage form.
6. The pharmaceutical composition according to Claim 5 wherein the unit dosage form is selected from the group consisting of a tablet and a capsule.
7. The pharmaceutical composition according to Claim 1 wherein the atorvastatin contains at least some partially or completely disordered form of atorvastatin or a
20 pharmaceutically acceptable salt thereof.
8. The pharmaceutical composition according to Claim 5 wherein the unit dosage form, after storage at 40°C and 75% relative humidity for 4 weeks, contains not more than about 1% total impurities and/or degradants based on area percent of drug related HPLC peaks.
- 25 9. The pharmaceutical composition according to Claim 5 wherein the unit dosage form, after storage at 40°C and 75% relative humidity for 4 weeks, contains not more than about 1% of atorvastatin lactone as calculated by area integration of HPLC peaks.
10. The pharmaceutical composition according to Claim 1 wherein the composition
30 comprises a diluent.
11. The pharmaceutical composition according to Claim 10 wherein said diluent has a mean particle size between about 20 and 200 μm .
12. The pharmaceutical composition according to Claim 10 wherein said diluent has a mean particle size between 40 and 150 μm .

13. The pharmaceutical composition according to Claim 1 wherein said composition shows a granulation factor of between about 0.4 and 1.0.
14. The pharmaceutical composition according to Claim 1 wherein said composition shows a granulation factor of between about 0.5 and 1.0.
- 5 15. The pharmaceutical composition according to Claim 1 wherein said composition shows a granulation factor of between about 0.6 and 1.0.
16. The pharmaceutical composition of Claim 1 wherein said composition comprises greater than 40% (w:w) of a diluent or combination of diluents wherein said diluent or combination of diluents have a granulation factor between 0.4 and 1.0
10 when tested alone with atorvastatin.
17. The pharmaceutical composition according to Claim 12 wherein said diluent comprises greater than about 50% (w:w) of microcrystalline cellulose, lactose, sucrose, xylitol or calcium phosphate dibasic.
18. The unit dosage form according to Claim 5 wherein said unit dosage form
15 produced therein shows a relative standard deviation for active drug per unit dosage form of less than 7.8% when said unit dosage form is prepared at a rate greater than about 10,000 unit dosage forms per hour per unit dosage form per machine.
19. The unit dosage form according to Claim 5 wherein said unit dosage form
20 produced therein shows a relative standard deviation for active drug per unit dosage form of less than 6.0% when said unit dosage form is prepared at a rate greater than about 10,000 unit dosage forms per hour per unit dosage form per machine.
20. The unit dosage form according to Claim 5 wherein said dosage form also
25 contains at least one active drug in addition to the atorvastatin.
21. The unit dosage form according to Claim 20 wherein said active drug in addition to the atorvastatin includes torcetrapib or amlodipine and pharmaceutically acceptable salts thereof.
22. A method for preparing a dry-granulated pharmaceutical composition of
30 atorvastatin comprising:
 - a. combining atorvastatin or a pharmaceutically acceptable salt thereof and one or more excipients suitable for use in a dry granulation step;
 - b. blending the mixture together in a mixer;
 - c. compressing the mixture;
 - 35 d. milling, grinding or sieving the compressed material;

- e. optionally adding additional excipients and mixing the combination to form the composition.

- 23. The method according to Claim 22 wherein said compression is carried out using a roller compactor.
- 5 24. The method according to Claim 22 wherein said compression is carried out using a tablet press.
- 25. The method according to Claim 22 wherein said compression provides a material having a tensile strength of about 0.55 to about 8 MPa.
- 10 26. The method according to Claim 22 wherein said compression provides a material having a tensile strength of about 0.8 to about 6 MPa.
- 27. The method according to Claim 22 wherein said compression provides a material having a solid fraction of between about 0.55 and about 0.85.
- 28. The method according to Claim 22 wherein said compression provides a material having a solid fraction of between about 0.60 and about 0.80.
- 15 29. The method according to Claim 22 wherein said milling, grinding or sieving provides a material wherein less than about 30% (w:w) of the material passes through a 200 mesh sieve.
- 30. The method according to Claim 22 wherein said milling, grinding or sieving provides a material wherein greater than about 70% (w:w) of the material passes through a 60 mesh sieve.
- 20 31. The method according to Claim 22 wherein the material after milling, grinding, or sieving in step (d) provides a granulation factor of between about 0.4 and about 1.0.
- 32. The method according to Claim 22 wherein the material after milling grinding, or sieving in step (d) provides a granulation factor of between about 0.5 and about 1.0.
- 25 33. The method according to Claim 22 wherein the material after milling grinding, or sieving in step (d) provides a granulation factor of between about 0.6 and about 1.0.
- 30 34. The method according to Claim 22 wherein the composition is used in the preparation of tablets or capsules.
- 35 35. The method according to Claim 34 wherein said tablets or capsules produced therein show a relative standard deviation for active drug per unit dosage form of less than 7.8% when said unit dosage forms are prepared on a tablet press or capsule filling machine at a rate greater than about 10,000 tablets or capsules per hour per unit dosage form per machine.

- 5 36. The method according to Claim 34 wherein said tablets or capsules produced therein show a relative standard deviation for active drug per unit dosage form of less than 6.0% when said unit dosage forms are prepared on a tablet press or capsule filling machine at a rate greater than 10,000 tablets or capsules per hour per unit dosage form per machine.
37. The method according to Claim 22 wherein said atorvastatin comprises at least some amount of a partially or completely disordered form of atorvastatin or a pharmaceutically acceptable salt thereof.
- 10 38. The method of preparing a unit dosage form containing atorvastatin and at least one other active drug wherein the composition prepared according to the method of Claim 22 is combined with at least one other active drug and optionally additional excipients.
39. The method of treating hypercholesterolemia and/or hyperlipidemia, osteoporosis, benign prostatic hyperplasia, and Alzheimer's disease comprising administering a therapeutically effective amount of the pharmaceutical composition of Claim 1.
- 15 40. A kit for achieving a therapeutic effect in a mammal comprising a therapeutically effective amount of dry-granulated atorvastatin or a pharmaceutically acceptable salt thereof step in a unit dosage form, and a container for containing said dosage form.
- 20 41. The kit according to Claim 39 containing at least some partially or completely disordered form of atorvastatin or a pharmaceutically acceptable salt thereof.
42. The kit according to Claim 39 wherein the unit dosage form is selected from the group consisting of a tablet or a capsule.
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